


Acute-onset polyradiculoneuropathy after SARS-CoV2 vaccine in the West and North Midlands, United Kingdom

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Abstract

Introduction/Aims: We aimed to determine whether specific severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) vaccines may be associated with acute-onset polyradiculoneuropathy and if they may result in particular clinical presentations.

Methods: We retrospectively reviewed records of all persons presenting with acute-onset polyradiculoneuropathy from January 1, 2021, to June 30, 2021, admitted to two Neuroscience centers, of the West and North Midlands, United Kingdom. We compared subjects with previous SARS-CoV2 vaccine exposure with a local cohort of persons with acute-onset polyradiculoneuropathy admitted between 2005 and 2019 and compared admission numbers for the studied time frame with that of the previous 3 years.

Results: Of 24 persons with acute-onset polyradiculoneuropathy, 16 (66.7%) presented within 4 weeks after first SARS-CoV2 vaccine. Fourteen had received the AstraZeneca vaccine and one each, the Pfizer and Moderna vaccines. The final diagnosis was Guillain-Barré syndrome (GBS) in 12 and acute-onset chronic inflammatory demyelinating polyneuropathy in 4. Among AstraZeneca vaccine recipients, facial weakness in nine persons (64.3%), bulbar weakness in seven (50%), and the bifacial weakness and distal paresthesias GBS variant in three (21.4%), were more common than in historical controls ($P = .01$; $P = .004$, and $P = .002$, respectively). A 2.6-fold (95% confidence interval: 1.98–3.51) increase in admissions for acute-onset polyradiculoneuropathy was noted during the studied time frame, compared to the same period in the previous 3 years.

Discussion: Despite a low risk, smaller than that of SARS-CoV2 infection and its complications, exposure to the first dose of AstraZeneca SARS-CoV2 vaccine may be a risk factor for acute-onset polyradiculoneuropathy, characterized by more common cranial nerve involvement.

Abbreviations: CI, confidence interval; CIDP, chronic inflammatory demyelinating polyneuropathy; CSF, cerebrospinal fluid; EMA, European Medicines' Agency; GBS, Guillain-Barré syndrome; ICU, intensive care unit; MHRA, Medicines and Healthcare products Regulatory Agency; SARS-CoV2, severe acute respiratory syndrome coronavirus 2; UK, United Kingdom; VITT, vaccine-induced thrombosis and thrombocytopenia.

Lay Khoon Loo and Omar Salim contributed equally to this study.

KEYWORDS

chronic inflammatory demyelinating polyradiculoneuropathy, Guillain-Barré syndrome, polyradiculoneuropathy

1 | INTRODUCTION

As of June 30, 2021, an estimated 24.6 million first doses of the AstraZeneca, 19.1 million of the Pfizer/BioNTech, and 1.0 million of the Moderna SARS-CoV2 vaccines, had been administered in the United Kingdom (UK).¹ The UK Medicines and Healthcare products Regulatory Agency (MHRA) has identified a possible link between thrombosis and thrombocytopenia and the AstraZeneca SARS-CoV2 vaccine.¹ There are few reports of Guillain-Barré syndrome (GBS) after the first dose of SARS-CoV2 vaccine.^{2–6} The majority relate to the AstraZeneca vaccine.

We performed a retrospective study of all patients presenting with acute-onset polyradiculoneuropathy to our two neuroscience centers in the West and North Midlands, United Kingdom, between January 1, 2021, and June 30, 2021. We aimed to compare admission numbers for acute-onset polyradiculoneuropathy with those for the same period during the previous 3 years. We also aimed to ascertain the frequency of exposure to the first dose of any SARS-CoV2 vaccine in the 4 week preceding onset of polyradiculoneuropathy and compare demographic and clinical features of post-SARS-CoV2 vaccine presentations with a local cohort of subjects with GBS admitted between 2005 and 2019.

2 | METHODS

We retrospectively searched our institutional databases for all patients aged ≥ 16 y with a new diagnosis of acute-onset polyradiculoneuropathy (GBS or acute-onset chronic inflammatory demyelinating polyradiculoneuropathy [CIDP], meeting diagnostic criteria^{7,8}), between January 1, 2021, and June 30, 2021.

Electronic patient records were reviewed for demographic details, clinical characteristics and progression, cerebrospinal fluid (CSF) analysis and electrophysiology. Other antecedent events and their timing were determined.

All patients with a new diagnosis of GBS or acute-onset CIDP who had received a first dose of any SARS-CoV2 vaccine in the preceding 4 weeks before onset of neurological symptoms were identified. Vaccine type and delay to onset from vaccine administration was documented. Electrophysiological subtype was determined at initial presentation for GBS, as per recent criteria,⁹ as was fulfillment of criteria for CIDP in patients with a subsequent chronic disease course.⁸

We compared demographic and clinical characteristics of post-SARS-CoV2 vaccine cases with a local cohort of 114 consecutive subjects with GBS admitted pre-SARS-CoV2 pandemic, between 2005 and 2019 at University Hospitals Birmingham, United Kingdom. We

also compared our combined numbers of institutional admissions for GBS during the studied time frame with the same period in the previous 3 years.

Comparison of proportions was performed by Fisher exact tests and comparison of means by independent *T*-tests, after normal distribution of data was confirmed.

This work was part of institutional audits on inflammatory neuropathy during the SARS-CoV2 pandemic and, thus, did not require Ethics Committee approval in the United Kingdom.

3 | RESULTS

Admissions to our two centers for acute-onset polyradiculoneuropathy from January 1, 2021, to June 30, 2021, showed a 2.7-fold increase compared with the same period in 2020 (9–24), a 3.4-fold increase compared with the same period in 2019 (7–24), and a 2-fold increase compared with the same period in 2018 (12–24). The increase in admissions in the studied period was, hence, 2.6-fold (95% CI: 1.98–3.51) compared with the average for the same period in the previous 3 years. This was consistent in both centers.

Of a total of 24 persons diagnosed with acute-onset polyradiculoneuropathy between January 1 and June 30, 2021, 16 (66.7%) had received the first dose of any SARS-CoV2 vaccine in the preceding 4 weeks before symptom onset.

Demographic and clinical characteristics of persons with acute-onset polyradiculoneuropathy following a first dose SARS-CoV2 vaccine are provided in Table 1. Mean time of onset after vaccination was 14.4 days (SD: 6.8). All but two had received the AstraZeneca vaccine. None reported antecedent infections or vaccinations. Electrophysiological results are detailed in Table 1. The subject with equivocal electrophysiology was diagnosed with classic GBS with quadriparesis, areflexia, and bifacial weakness. CSF protein was 210 mg/dL. The subject with normal electrophysiology was diagnosed clinically with the bifacial weakness and distal paresthesias GBS variant and had a CSF protein of 89 mg/dL. All 16 persons were treated with intravenous immunoglobulin at initial presentation. Four persons (25%) had a subsequent clinical course and electrophysiology meeting criteria for acute-onset CIDP.⁸ These subjects were subsequently successfully re-treated with intravenous immunoglobulin in two, corticosteroids in one, and plasma exchanges in two. Outcomes are detailed in Table 1.

Comparative analysis of demographic and clinical features in the 14 persons with acute polyradiculoneuropathy presenting after the first dose of the AstraZeneca vaccine with a local cohort of 114 consecutive persons with GBS who attended our institution between 2005 and 2019 at University Hospitals Birmingham, United Kingdom, is shown in

TABLE 1 Characteristics of 16 persons with acute-onset polyradiculoneuropathy within 4 wk of any first dose of SARS-CoV2 vaccination

Mean age (SD) (y)	57.2 (9.5)
Gender distribution	9 males, 7 females
Vaccine exposure	
AstraZeneca	14 (87.5%)
Pfizer	1 (6.3%)
Moderna	1 (6.3%)
Clinical subtype	
Classic GBS	12 (75%)
Bifacial weakness and distal paresthesias	3 (18.8%)
Pharyngocervicobrachial variant	1 (6.3%)
Clinical features	
Motor weakness	14 (87.5%)
Hypo/areflexia	13 (81.3%)
Facial weakness	9 (56.3%)
Bulbar weakness	8 (50%)
Dysautonomia	1 (6.3%)
Electrophysiological subtype	
AIDP	11 (68.8%)
Axonal	1 (6.3%)
Equivocal	1 (6.3%)
Normal	1 (6.3%)
Not done	2 (12.5%)
Mean CSF protein (SD) (mg/dl)	180 (115)
Antiganglioside antibody positivity	0/8 (0%)
ICU admission	4 (25%)
Mechanical ventilation	3 (18.8%)
Ability to walk unaided at discharge	8 (50%)
In-hospital mortality	1 (6.3%)

Abbreviation: AIDP, acute inflammatory demyelinating polyneuropathy.

Table 2. Persons presenting with acute-onset polyradiculoneuropathy after first AstraZeneca SARS-CoV2 vaccine had more frequent facial and bulbar weakness, than historical controls and more commonly had the bifacial weakness and distal paresthesias GBS variant.

4 | DISCUSSION

We found that our centers experienced a 2.6-fold increase in number of admissions for GBS during the study period, compared to the same period in the previous 3 years. We believe it is possible that this may be due to the cases of polyradiculoneuropathy post-SARS-CoV2 vaccination. Reduced exposure to other pathogens through distancing measures and hand hygiene was postulated as cause for reduced GBS incidence in the first months of the pandemic in 2020,¹⁰ but our comparative admission rates in 2018 and 2019 do not support this.

Facial weakness, in this cohort, was exclusively present in recipients of the AstraZeneca vaccine. We found that persons presenting with acute-onset polyradiculoneuropathy within 4 weeks after first AstraZeneca SARS-CoV2 vaccine more commonly presented with facial and bulbar weakness, compared with GBS patients seen between 2005 and 2019. They also more commonly had the bifacial weakness and distal paresthesias GBS variant. All seven cases reported from India after the AstraZeneca vaccine also had facial weakness.² Similarly, four cases of the GBS variant with facial weakness with distal paresthesias were reported from another UK center following the AstraZeneca vaccine.³ However, we observed no differences with historical controls in demographic or other clinical characteristics, rates of intensive care unit (ICU) admission, or ventilator support.

Most cases identified in our study (87.5%) occurred after the AstraZeneca vaccine. Despite a few reports, there is to date no causation established between this vaccine and GBS. Recently, the European Medicines' Agency (EMA) safety committee has recommended a change in product information for the AstraZeneca vaccine to include a warning about cases of GBS reported following vaccination.¹¹ Although such precautionary measures are not unusual, the situation with SARS-CoV2 vaccines, as opposed to others previously, differs in that reported cases of polyradiculoneuropathy, including ours, suggest a possible risk with one vaccine type. A similar example is vaccine-induced thrombosis and thrombocytopenia (VITT) associated with the AstraZeneca vaccine, initially considered uncertain,¹² but now postulated to have an immunological pathogenesis.¹³ Whereas no specific measures for younger persons were initially taken,¹⁴ risk stratification by age was subsequently implemented in the United Kingdom.¹⁵

The mechanisms involved in post-vaccination inflammatory neuropathy may relate to antibody production cross-reacting with neural components. This may involve the SARS-CoV2 spike protein. Of note, in addition to the AstraZeneca vaccine, the Johnson&Johnson/Janssen vaccine, has also recently been reported to precede GBS in 100 patients.¹⁶ This has not been the case in similar proportions with mRNA vaccines. It is also possible that the immune target in the cases following AstraZeneca vaccination may be related to the adenovirus vector, which may explain the rarity of cases after mRNA vaccines.¹⁷ In the absence of further data, the possibility of specific immune mechanisms in polyradiculoneuropathy, as postulated for VITT in relation to adenovirus-DNA vaccines cannot, therefore, be excluded.

Our study is limited by its retrospective design and the small region covered by our institutions. Random clustering may be argued as a potential explanation. However, occurrence predominantly after the first dose of the AstraZeneca vaccine, clinical differences including more common cranial involvement, and increased admission rates for acute-onset polyradiculoneuropathy at our institutions from the onset of the vaccination campaign, raise the need for further studies.

Temporal association does not imply causality.¹⁸ The overwhelmingly beneficial effect of vaccines on the current SARS-CoV2 pandemic clearly and repeatedly needs emphasizing,¹⁹ in comparison to the low risk of adverse events, including GBS or acute-onset CIDP. However, at

TABLE 2 Comparison of acute-onset polyradiculoneuropathy after first dose of the AstraZeneca SARS-CoV2 vaccine with consecutive historical controls

	Persons with post-SARS-CoV2 vaccine acute-onset polyradiculoneuropathy January 1, 2021, to June 30, 2021	Historical controls with acute-onset polyradiculoneuropathy 2005–2019	P Value
Number	14	114	NA
Mean age (SD) (y)	57 (10)	52.1 (19.3)	.14
Gender	8 males; 6 females	75 males, 39 females	.56
Motor weakness	12 (87.5%)	94 (82.5%)	1.0
Facial weakness	9 (64.3%)	31 (27.2%)	.01
Bulbar weakness	7 (50%)	16 (14%)	.004
Dysautonomia	1 (7.1%)	14 (12.3%)	1.0
Classic GBS subtype	10 (71.4%)	99 (86.8%)	.22
Bifacial weakness and distal paresthesias GBS subtype	3 (21.4%)	0 (0%)	.002
Pharyngocervicobrachial (PCB) GBS variant	1 (7.1%)	0 (0%)	.10
ICU admission	4 (28.6%)	27 (23.7%)	1.0
Ventilation	3 (21.4%)	20 (17.5%)	.72
Ability to walk unaided at discharge	8 (57.1%)	40 (42.1%)	.39
In-hospital mortality	1 (7.1%)	7 (6.1%)	1.0

Bold values are statistically significant results of the study.

the time of revision of this manuscript, our findings are supported by a self-controlled nationwide case series UK study, published on October 25, 2021.²⁰ This analysis, which used the English National Immunization Database of SARS-CoV2 vaccinations linked to hospital admission data, found similar results to ours, with a 2.04-fold increased risk for GBS (95% confidence interval [CI]: 1.60–2.60) within 28 days after AstraZeneca vaccine administration, but not after the Pfizer vaccine. In addition, this study described a 5.05-fold increased GBS risk after a SARS-CoV2 positive test (95% CI: 3.00–9.18), in contrast to another analysis from the UK. Knowledge of SARS-CoV2 vaccines as well as SARS-CoV2 infection itself in relation to peripheral nerve complications appears to be evolving.

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CONFLICT OF INTEREST

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ETHICAL PUBLICATION STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

DATA AVAILABILITY STATEMENT

Anonymised data available at reasonable request.

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